

Amendments to the Specification

Please amend the specification as follows:

a) Please replace the existing paragraph on page 7, lines 18-21 with the following paragraph:

Figure 11 shows the primers used (3NT5'OST [SEQ ID NO:[] 17]; 3NT3'OHT [SEQ ID NO:[] 18]; 3NT5'KHT [SEQ ID NO:[] 19]; 3NT3'KST [SEQ ID NO:[] 20]; 1NT5'[[OSI]] ORI [SEQ ID NO: [] 21]; 1NT3'Ori(s) [SEQ ID NO:[[6]] 22]; 1NT5'KAN [SEQ ID NO:[[11]] 23]; 1NT3'KAN [SEQ ID NO:[[12]] 24).

b) Please replace the existing paragraph on page 34, lines 1-6 with the following paragraph:

The vector/insert hybrid molecule depicted in Figure 10 was generated as follows. The ori-containing vector fragment was amplified from pET 19b (Novagen, Madison, WI) using primers (lower case letters indicate RNA residues; upper case letters indicate DNA residues) 5'OST (5'-CTGCTAAGTGAGcucGACAGATCGCTGAGATAGGTGC; SEQ ID NO:[[5]] 7) and 1N3'Ori(s)(5'-AAGCTTGCTAAGTA_gGGCGTTTTTCCATAGGCTCCG; SEQ ID NO:[[6]] 8)

c) Please replace the existing paragraph on page 34, lines 7-11 with the following paragraph:

The vector fragment containing the Kanamycin resistance gene was amplified from pCR2.1 Topo (Invitrogen, Carlsbad, CA) using primers 1NT5'KAN (5'-CTACCTAGCAAGCTuCTATCTGGACAAGGGAAAACG; SEQ ID NO:[[7]] 9) and T7 3'KAN (5'-CCCTATAGTGAGTCGTATTA_aGGCGAAAACCTCTCAAGGATC; SEQ ID NO:[[8]] 10).

d) Please replace the existing paragraph on page 34, lines 12-16 with the following paragraph:

The insert fragment containing the luciferase gene was amplified from pGI II basic (Promega, WI) using primers tCS1 (5' TTAATACGACTCACTATAGGGGATGGAAGACGCCAAAAACATA; SEQ ID NO: [[9]] 11) and tCS8 (5'- GAGCTCACTTAGCAGTTACAATTTGGACTTTCCGCC; SEQ ID NO: [[10]] 12).

e) Please replace the existing paragraph on page 35, line 17 - page 37, line 5 with the following paragraph:

Those of ordinary skill in the art will appreciate that, as with Example 6, the ROC technique described in this Example utilizes primers containing internal ribonucleotide residues (in one case, 3 residues were used; in other cases only one) flanked by DNA residues. The overhangs created in these ROC PCR reactions, therefore, have only a single "ribo" residue; other overhang residues are DNA. In separate experiments, we have demonstrated that any individual ribonucleotide (i.e., rA, rG, rU, or rC) can act effectively to block extension of a complimentary strand by an appropriate DNA polymerase, so that overhangs are created (see, for example, Example 6). We have also showed that single 3'-~~O-methyl~~ 2'-O-methyl residues are similarly effective. Primers containing 3'-~~O-methyl~~ 2'-O-methyl residues can often be synthesized more easily (e.g., due to higher coupling efficiencies) than those containing ~~ribonucleotides~~ ribonucleotides, and will generally be more stable, so that they are preferred for many applications.

f) Please replace the existing paragraph on page 36, line 19 – page 37, line 9 with the following heading:

The following chimeric RNA/DNA primers were purchased from Oligo's Etc. (Willsonville, OR): (ribonucleotides are in lower case)

1NT 5'KAN-CTACCTAGCAAGCT_uCTATCTGGACAAGGGAAAACG (SEQ ID NO:13)

1NT 3'KAN-GAGCTCACTTAGCAAGGCGAAAACCTCTCAAGGA (SEQ ID NO:14)

1NT5' Ori- ~~TTGCTAAGTGAGCU~~_cGACAGATCGCTGAGATAGGTGC
TTGCTAAGTGAGCT_cGACAGATCGCTGAGATAGGTGC (SEQ ID NO:15) 1N3' Ori(s) 1NT3' Ori(s) -

AAGCTTGCTAAGTA_gGGCGTTTTTCCATAGGCTCCG (SEQ ID NO:16)

Primers 1NT 5'KAN and 1NT 3'KAN were used to amplify the Kan fragment from pCR 2.1 Topo (Invitrogen, Carlsbad, CA). Primers 1NT5' Ori and ~~1N3' Ori(s)~~ 1NT3' Ori(s) were used to amplify the Ori fragment from pET 19b (Novagen, Madison, WI). The following cycles were performed: one cycle of 95°, 3', 48-60°, 2', 72°, 8'; followed by 35 cycles of 95°, 30sec, 48-60°, 30 sec, 72°, 3' for Ori fragment, 4.5' for Kan and Luc fragments. A final cycle with an 8' 72° step was performed in all cases.